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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,513	01/15/2004	Marc Lemaire	Serie 6093	5797

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EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/758,513	LEMAIRE, MARC	
	Examiner	Art Unit	
	Ernst V. Arnold	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *na* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/15/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

The Examiner acknowledges receipt of application number 10/758,513 filed on 01/15/2004. Claims 1-15 have been canceled in a preliminary amendment and claims 16-41 have been added. Accordingly, claims 16-41 are presented for examination on the merits.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Drawings

The subject matter of this application admits of illustration by a drawing(s) (Figures 1-5) to facilitate understanding of the invention. Applicant is required to furnish a drawing(s) under 37 CFR 1.81(c). No new matter may be introduced in the required drawing. Each drawing sheet submitted after the filing date of an application must be

labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 33 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating post-ischemic brain cell deterioration via administering an effective amount of the instantly claimed composition to a subject in need thereof, does not reasonably provide enablement for preventing post-ischemic brain cell deterioration by such *in vivo* administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

An analysis of whether the scope of a particular claim is actually supported by the disclosure in a patent application requires a determination of whether the disclosure, at the time of filing, contained sufficient information regarding the subject matter of the claim at issue so as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. In re Wands, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988). Therefore, the test of enablement is not whether experimentation is necessary, but rather, if experimentation is in fact necessary, whether it is reasonably considered to be undue. In re Angstadt, 190 USPQ 214, 219 (CCPA 1976).

Determining the issue of enablement with respect to a claim is a question of law based on underlying factual findings. In re Vaeck, 20 USPQ 2d 1438, 1444 (Fed. Cir. 1991). More particularly, there are many factors to be considered in determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, and whether any necessary experimentation is reasonably considered to be "undue." See In re Wands at page 1404. MPEP § 2164.01(a). The Court in In re Wands set forth the following factors to be considered, which include, without limitation, the: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure.

The specification merely discloses, without more, that rats subjected to transient focal cerebral ischemia and subsequently made to inhale a mixture of gases makes it possible to reduce the total volume of infarction. However, Applicant is purporting to prevent or cure the pathological manifestation and clinical presentation of cerebral ischemia in a mammal suffering therefrom or susceptible thereto. As a result, the claims are broader in scope than the enabling disclosure.

The nature of the invention is directed to a composition and method of preventing post-ischemic brain cell deterioration in a mammal utilizing said composition.

The relative level of skill possessed by one of ordinary skill in the art of formulating compositions for not only treating, but also attempting to discover a prevention or cure for, dehydration in a mammal is relatively high, as a majority of lead investigators conducting scientific research and development in this particular technological area, as of the effective filing date of the instant application, possess an M.D. and/or a Ph.D. in a scientific discipline such as organic synthetic chemistry, medicinal chemistry, biochemistry, pharmacology, biology or the like.

An extraordinary degree of unpredictability, not to mention a great deal of uncertainty due to a distinct lack of knowledge of the skilled artisan, existed in the state of the prior art regarding how to absolutely prevent post-ischemic brain cell deterioration in a mammal.

The applicant provides guidance on how to treat post-ischemic brain cell deterioration but there is no data provided on the prevention of post-ischemic brain cell deterioration.

The applicant provides one example on the treatment of rats *after* an ischemic event.

Since a great deal of uncertainty, due to a distinct lack of knowledge of the skilled artisan, existed in the state of the art at the time the instant application was filed, and because there was an extremely low level or degree of predictability in the art as of the effective filing date of the instant application, then the Applicant is required to provide in the specification additional guidance and direction with respect to how use the claimed subject matter in order for the application to be enabled with respect to the full scope of

the claimed invention. Although the instant specification discloses a composition and corresponding method for treating post-ischemic brain cell deterioration in a mammal, the specification utterly fails to provide scientific data and working embodiments with respect to a composition and corresponding method of absolutely preventing post-ischemic brain cell deterioration in a mammal.

As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation to reasonably and accurately determine whether the composition and corresponding method of the instant application does in fact prevent post-ischemic brain cell deterioration in a mammal.

In conclusion, it is readily apparent from the aforementioned disclosure, in conjunction with a corresponding lack of scientific data and working embodiments regarding the prevention of post-ischemic brain cell deterioration in a mammal utilizing said method, that one of ordinary skill in the art would therefore be required to conduct an undue amount of experimentation to reasonably and accurately extrapolate whether said composition and corresponding method would actually prevent post-ischemic brain cell deterioration in a mammal.

"Prevention" is defined in Webster's New World Dictionary as "to keep from happening; make impossible by prior action." See, Webster's New World Dictionary, 3rd College Ed., Webster's New World Dictionary Publishing, page 1067-1068 (1988) (Reference U). Applicant is advised that although claim language, such as "preventing" lack enablement under 35 U.S.C. § 112, first paragraph, phrases such as "reducing the incidence," "reducing the frequency," or "reducing the likelihood," etc. are considered by

the Office to be enabling, assuming of course that the specification in question has adequate written description and support for the asserted and claimed utility.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 16-18, 20-23, 26, 27, 30, 33-36, and 38-41 are rejected under 35 U.S.C. 102(a) as being anticipated by Homi et al. (Anesthesiology 2003, 99, 876-881).

Instant claim 16 is drawn to a composition comprising at least one component selected from the group consisting of: a) nitrous oxide, and b) a nitrous oxide donor. Instant claim 17 is drawn to the medicinal composition according to claim 16, wherein said composition further comprises at least one component selected from the group consisting of a) xenon, and b) a xenon donor. Instant claim 18 provides the limitation to instant claim 16 wherein the composition further comprises at least one gaseous component selected from the group consisting of: a) oxygen, b) nitrogen, and c) argon.

Homi et al. disclose the neuroprotective effect of xenon administration during transient middle cerebral artery occlusion in mice (Abstract). Homi et al. provide gaseous compositions and methods of administrating the gas to a subject (See: Materials and Methods page 876). Homi et al. administered three gas mixtures to mice subjected to 60 minutes of middle cerebral artery occlusion: 1) 70% xenon and 30%

oxygen; 2) 70% nitrous oxide and 30% oxygen; and 3) 35% xenon and 35% nitrous oxide and 30% oxygen (Page 877, left column, last paragraph; page 878, under results; Table 2, page 878 upper right and corner and Figure 1, page 879, for example). The Examiner interprets about 75% of instant claim 23 to mean 75% ± 7.5% which provides a range of 67.5% to 82.5% nitrous oxide. The amount of nitrous oxide used in the disclosure of Homi et al. (70%) is within the scope of the instant invention and would therefore constitute an effective amount. The disclosure of Homi et al. is deemed to meet the limitations of instant claims 16-18, 20-23, 26, 27, 30, 33-36, and 38-41.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16, 18, 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Bracken (US 3,876,773).

Bracken discloses an anesthetic gas mixture consisting of 40 to 60% nitrous oxide, 3 to 10% carbon dioxide and 30 to 55% oxygen (Abstract; column 1, lines 30-38 and claim 1). The disclosure of Bracken meets the limitations of a medicinal composition comprising inhalable gaseous nitrous oxide (instant claims 16, 20 and 21) and oxygen (instant claim 18). The composition of Bracken is comprised of the same

components as the instantly claimed invention and therefore would have the same properties as the instantly claimed invention; namely, treating post-ischemic brain cell deterioration.

Claim Rejections - 35 USC § 102

Claims 16, 18-21, 23-25, 28, 30-34, 36, 37, and 39-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Mondain-Monval (US 4,820,258).

Mondain-Monval disclose a gaseous mixture comprising oxygen, nitrous oxide, and an optional inert gas, such as nitrogen or xenon, to be administered by inhalation to a patient (See: Abstract; Column 1, lines 59-62; column 2, lines 10-14 and lines 22-25; and claims 4 and 5). This reads on instant claims 16 and 18-21. Please note that the composition of Mondain-Monval meets the instant claim limitations and would inherently perform the functional effects of providing neuroprotective action in the brain of the instantly claimed invention. The volume of nitrous oxide is between 50 and 80% by volume and at least about 20% by volume of oxygen Column 1, lines 66-68 and column 2, lines 1-2). The gaseous mixture can be in the form of a ternary mixture consisting of oxygen, nitrous oxide and the complement to 100% by volume by an inert gas selected from nitrogen, argon, krypton, xenon and helium (Column 2, lines 10-14 and claims 2-5). For example, if a gaseous composition were comprised of 50% nitrous oxide and 20% oxygen then the complement in xenon would be 30%. Thus, instant claims 17, 22-30 are anticipated. Mondain-Monval disclose that the gaseous mixtures can be prepackaged under pressures compatible with maintaining the mixtures in gaseous form (Column 2, lines 15-17). The Examiner interprets this to mean the gaseous mixture in a

pressurized gas container therefore anticipating instant claim 31. Gas bottles and gas cylinders are synonymous and are known in the art as typical storage containers for pressurized gases. In the absence of evidence to the contrary, the prepackaged gaseous mixtures of Mondain-Monval are gas bottles/cylinders and anticipate instant claim 32.

Instant claim 33 is drawn to a method comprising administrating a medicinal composition comprising nitrous oxide or nitrous oxide donor.

Mondain-Monval disclose the administration of a gaseous mixture comprising at least about 50% by volume of nitrous oxide to a patient by inhalation thus anticipating instant claims 33 and 34. Mondain-Monval anticipate the addition of an inert gas to the nitrous oxide and point out xenon therefore reading on instant claim 35 (Claim 5). Mondain-Monval claim the method of administration of a gaseous mixture wherein the gasesous mixture contains from about 50 to 80% by volume nitrous oxide, at least 20% by volume oxygen (Claims 2 and 3). Further, Mondain-Monval anticipate the addition of an inert gas to the oxygen and nitrous oxide (Claim 4). The inert gas is selected from the group consisting of nitrogen, argon, krypton, xenon and helium (Claim 5). The Examiner interprets about 75% of instant claim 23 to mean 75% ± 7.5% which provides a range of 67.5% to 82.5% nitrous oxide. Therefore, the disclosure of Mondain-Monval is within the scope of the instant invention and would constitute an effective amount. The Examiner interprets that inhalation means that the components to be inhaled are in gaseous form and any subject inhaling the gaseous mixture would receive any benefit from doing so The Examiner interprets about 75% of instant claim 23 to mean 75% ±

7.5% which provides a range of 67.5% to 82.5% nitrous oxide. Thus, instant claims 36-41 are anticipated.

Claim Rejections - 35 USC § 102

Claims 16, 18, 20, 21, 23-25, 28, 30, 33, 34, 36, 37 and 39-41 rejected under 35 U.S.C. 102(b) as being anticipated by Jevtovic-Todorovic et al. (Nature Medicine 1998, 4, pages 460-463).

Jevtovic-Todorovic et al. disclose a study designed to test the ability of nitrous oxide to protect neurons against excitotoxic action of N-methyl-D-aspartate (Right column, page 460). Jevtovic-Todorovic et al. treated adult rats with various gas mixtures of nitrous oxide and oxygen ranging from 20%, 40%, 80%, 150% and 180% nitrous oxide, for example (Page 462, top left column and page 463, methods). Thus, instant claims 16, 18, 20, 24, 25, 28, 33, 34, 36, 39, and 41 are anticipated. The mice were made to inhale the gas mixtures inside a chamber hence reading on instant claims 21 and 30 (Page 460, lower right column and page 463, methods). The amount of nitrous oxide used in the disclosure of Jevtovic-Todorovic et al. (80% N_2O and 20% O_2) is within the scope of the instant invention and would therefore constitute an effective amount therefore reading on instant claims 23 and 40. Jevtovic-Todorovic et al. suggest that administration of nitrous oxide may provide neuroprotection against cerebral ischemic events that sometimes accompany surgery (Page 463, left column).

Claim Rejections - 35 USC § 102

Claims 16, 18, 19, 20, 21, 28, 29, 30, 33, 34, 36, 37, 39 and 41 rejected under 35 U.S.C. 102(b) as being anticipated by Vanderipe WO 93/06869.

Vanderipe discloses gas mixtures with the intended use as ultrasound imaging reagents (Abstract). Vanderipe discloses inhalable gas mixture compositions that are 20% oxygen, 20% nitrogen and 60% nitrous oxide thus reading on instant claims 16, 18, 19, 20, 21, 28, 29 and 30 (Page 8, lines 12 and 13; page 9, lines 4-12; and claims 1, 5, 9 and 13). Vanderipe discloses methods of administration of the gas mixture compositions (See: page 8 line 21 through page 10, line18). Subjects receiving the gas mixture of Vanderipe would inherently receive all medical benefits, including treatment of post-ischemic brain cell deterioration, that are characterized by the mixture of gases therefore reading on instant claims 33, 34, 36, 37, 39 and 41.

Conclusion

Claims 16-41 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

EVA

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